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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/681,508 | 04/18/2001 | Yun Lin | NEX 89 | 4609 |

25871 7590 10/17/2003

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| EXAMINER | |
|---|---|
| FORMAN, BETTY J | |
| **ART UNIT** | **PAPER NUMBER** |
| 1634 | |

DATE MAILED: 10/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/681,508 | LIN ET AL. | |
| | Examiner | Art Unit | |
| | BJ Forman | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *7 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *29-34,36-50 and 52-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-34,36-50 and 52-60* is/are rejected.

7)☒ Claim(s) *44, 60* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/01 9/0[illegible]*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7 July 2003 has been entered.

***Status of the Claims***

2. This action is in response to papers filed 7 July 2003 in which claims 29 and 45 were amended and claims 35 and 51 were canceled. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 19 November 2002 are withdrawn in view of the amendments and new grounds for rejection. All of the arguments have been thoroughly reviewed but are deemed moot in view of the new grounds for rejection. New grounds for rejection are discussed.

The examiner for this application has changed. Please address future correspondence to Examiner BJ Forman, Art Unit: 1634.

Claims 29-34, 36-50 and 52-60 are under prosecution.

***Claim Objections***

3. Claims 44 and 60 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Applicant is advised that should claims 29 and 45 be found allowable, claims 44 and 60 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 29-34, 36-50, 52-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al (U.S. Patent No. 5,853,984, issued 29 December 1998).

Regarding Claim 29, Davis et al disclose a method for detecting the presence of two or more target compounds (e.g. HNE wherein HNE is coated on beads thereby providing and detecting multiple HNE targets, Column 10, line 63-Column 11, line 4) in a substance which may contain said target compounds comprising: exposing a substance which may contain said target compounds to capture molecules, wherein each capture molecule binds specifically to a corresponding target compound, to form a capture molecule:target compound complex; removing the remainder of said substance from said capture molecule:target compound complexes; adding to said capture molecule:target compound complexes reporter molecules; wherein each reporter molecule binds specifically to a corresponding target compound to form a capture molecule:target compound:reporter molecule complex; and detecting said target compounds by detection of said capture molecule:target compound:reporter molecule complexes, wherein said detecting comprises detecting by flow cytometry; wherein said capture molecules, said reporter molecules or both are a nucleic acid ligand to said target compounds (Column 5, lines 7-23 and Example 1, Column 10, line 35-Column 14, line 39).

Regarding Claims 30-32, Davis et al disclose the method wherein said reporter molecule comprises a detection system i.e. fluorescein (Column 8, line 41-Column 9, line 5).

Regarding Claim 33, Davis et al disclose the method wherein the capture molecule is immobilized on a solid support (Column 9, line 24-37).

Regarding Claim 34, Davis et al disclose the method wherein the solid support is a microsphere particle i.e. bead (Column 10, lines 18-25 and 63-67).

Regarding Claim 36, Davis et al disclose the method wherein the targets are proteins e.g. HNE (Column 10, lines 18-54).

Regarding Claim 37, Davis et al disclose the method wherein the proteins are L-Selectin (Example 2, Column 14, lines 45-67).

Regarding Claim 38, Davis et al disclose the method wherein the capture molecules and reporter molecules are nucleic acid ligands (Column 9, lines 35-40).

Regarding Claim 39, Davis et al disclose the method wherein the capture molecules are nucleic acid ligands and the reporter molecules are proteins (Column 9, lines 35-55).

Regarding Claim 40, Davis et al disclose the method wherein the capture molecule and reporter molecule bind to non-overlapping sites i.e. bind simultaneously to the target (Column 9, lines 24-64).

Regarding Claim 41, Davis et al disclose the method wherein the reporter molecule binds to a site on the capture molecule:target complex (Column 9, lines 24-64).

Regarding Claims 42 and 43, Davis et al disclose the method wherein the substance is a biological fluid e.g. plasma or urine (Column 10, lines 7-11).

Regarding Claim 44, Davis et al disclose the method wherein the detection is achieved by flow cytometry (Column 9, lines 24-37).

Regarding Claim 45, Davis et al disclose a method for detecting the presence of two or more target compounds (e.g. HNE wherein HNE is coated on beads thereby providing and detecting multiple HNE targets, Column 10, line 63-Column 11, line 4) in a substance which may contain said target compounds comprising: identifying a nucleic acid ligand for each target compound from a candidate mixture (Column 5, line 63-Column 6, line 59); exposing a substance which may contain said target compounds to capture molecules, wherein each capture molecule binds specifically to a corresponding target compound, to form a capture molecule:target compound complex; removing the remainder of said substance from said capture molecule:target compound complexes; adding to said capture molecule:target compound complexes reporter molecules; wherein each reporter molecule binds specifically to a corresponding target compound to form a capture molecule:target compound:reporter molecule complex; and detecting said target compounds by detection of said capture molecule:target compound:reporter molecule complexes, wherein said detecting comprises detecting by flow cytometry; wherein said capture molecules, said reporter molecules or both

are a nucleic acid ligand to said target compounds (Column 5, lines 7-23 and Example 1, Column 10, line 35-Column 14, line 39).

Regarding Claims 46-48, Davis et al disclose the method wherein said reporter molecule comprises a detection system i.e. fluorescein (Column 8, line 41-Column 9, line 5).

Regarding Claim 49, Davis et al disclose the method wherein the capture molecule is immobilized on a solid support (Column 9, line 24-37).

Regarding Claim 50, Davis et al disclose the method wherein the solid support is a microsphere particle i.e. bead (Column 10, lines 18-25 and 63-67).

Regarding Claim 52, Davis et al disclose the method wherein the targets are proteins e.g. HNE (Column 10, lines 18-54).

Regarding Claim 53, Davis et al disclose the method wherein the proteins are L-Selectin (Example 2, Column 14, lines 45-67).

Regarding Claim 54, Davis et al disclose the method wherein the capture molecules and reporter molecules are nucleic acid ligands (Column 9, lines 35-40).

Regarding Claim 55, Davis et al disclose the method wherein the capture molecules are nucleic acid ligands and the reporter molecules are proteins (Column 9, lines 35-55).

Regarding Claim 56, Davis et al disclose the method wherein the capture molecule and reporter molecule bind to non-overlapping sites i.e. bind simultaneously to the target (Column 9, lines 24-64).

Regarding Claim 57, Davis et al disclose the method wherein the reporter molecule binds to a site on the capture molecule:target complex (Column 9, lines 24-64).

Regarding Claims 58 and 59, Davis et al disclose the method wherein the substance is a biological fluid e.g. plasma or urine (Column 10, lines 7-11).

Regarding Claim 60, Davis et al disclose the method wherein the detection is achieved by flow cytometry (Column 9, lines 24-37).

6. Claims 29-34, 36-50, 52-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al (WO 96/41019, published 19 December 1996).

Regarding Claim 29, Davis et al disclose a method for detecting the presence of two or more target compounds (e.g. HNE wherein HNE is coated on beads thereby providing and detecting multiple HNE targets, page 16, lines 1-7) in a substance which may contain said target compounds comprising: exposing a substance which may contain said target compounds to capture molecules, wherein each capture molecule binds specifically to a corresponding target compound, to form a capture molecule:target compound complex; removing the remainder of said substance from said capture molecule:target compound complexes; adding to said capture molecule:target compound complexes reporter molecules; wherein each reporter molecule binds specifically to a corresponding target compound to form a capture molecule:target compound:reporter molecule complex; and detecting said target compounds by detection of said capture molecule:target compound:reporter molecule complexes, wherein said detecting comprises detecting by flow cytometry; wherein said capture molecules, said reporter molecules or both are a nucleic acid ligand to said target compounds (page 7, lines 1-13 and Example 1, pages 15-21).

Regarding Claims 30-32, Davis et al disclose the method wherein said reporter molecule comprises a detection system i.e. fluorescein (page 12, lines 9-30).

Regarding Claim 33, Davis et al disclose the method wherein the capture molecule is immobilized on a solid support (page 13, lines 14-23).

Regarding Claim 34, Davis et al disclose the method wherein the solid support is a microsphere particle i.e. bead (page 15, lines 1-2 and page 16, lines 1-7).

Regarding Claim 36, Davis et al disclose the method wherein the targets are proteins e.g. HNE (page 14, lines 28-30 and page 15, lines 10-22).

Regarding Claim 37, Davis et al disclose the method wherein the proteins are L-Selectin (Example 2, page 22, lines 5-19).

Regarding Claim 38, Davis et al disclose the method wherein the capture molecules and reporter molecules are nucleic acid ligands (page 14, lines 4-6).

Regarding Claim 39, Davis et al disclose the method wherein the capture molecules are nucleic acid ligands and the reporter molecules are proteins (page 13, line 24-page 14, line 4).

Regarding Claim 40, Davis et al disclose the method wherein the capture molecule and reporter molecule bind to non-overlapping sites i.e. bind simultaneously to the target (page 13, line 14-page 14, line 13).

Regarding Claim 41, Davis et al disclose the method wherein the reporter molecule binds to a site on the capture molecule:target complex (page 14, lines 7-13).

Regarding Claims 42 and 43, Davis et al disclose the method wherein the substance is a biological fluid e.g. plasma or urine (page 14, lines 20-23).

Regarding Claim 44, Davis et al disclose the method wherein the detection is achieved by flow cytometry (page 13, lines 14-23).

Regarding Claim 45, Davis et al disclose a method for detecting the presence of two or more target compounds (e.g. HNE wherein HNE is coated on beads thereby providing and detecting multiple HNE targets, page 16, lines 1-7) in a substance which may contain said target compounds comprising: identifying a nucleic acid ligand (page 8, line 9-30); exposing a substance which may contain said target compounds to capture molecules, wherein each capture molecule binds specifically to a corresponding target compound, to form a capture molecule:target compound complex; removing the remainder of said substance from said capture molecule:target compound complexes; adding to said capture molecule:target compound complexes reporter molecules; wherein each reporter molecule binds specifically to

a corresponding target compound to form a capture molecule:target compound:reporter molecule complex; and detecting said target compounds by detection of said capture molecule:target compound:reporter molecule complexes, wherein said detecting comprises detecting by flow cytometry; wherein said capture molecules, said reporter molecules or both are a nucleic acid ligand to said target compounds (page 7, lines 1-13 and Example 1, pages 15-21).

Regarding Claims 46-48, Davis et al disclose the method wherein said reporter molecule comprises a detection system i.e. fluorescein (page 12, lines 9-30).

Regarding Claim 49, Davis et al disclose the method wherein the capture molecule is immobilized on a solid support (page 13, lines 14-23).

Regarding Claim 50, Davis et al disclose the method wherein the solid support is a microsphere particle i.e. bead (page 15, lines 1-2 and page 16, lines 1-7).

Regarding Claim 52, Davis et al disclose the method wherein the targets are proteins e.g. HNE (page 14, lines 28-30 and page 15, lines 10-22).

Regarding Claim 53, Davis et al disclose the method wherein the proteins are L-Selectin (Example 2, page 22, lines 5-19).

Regarding Claim 54, Davis et al disclose the method wherein the capture molecules and reporter molecules are nucleic acid ligands (page 14, lines 4-6).

Regarding Claim 55, Davis et al disclose the method wherein the capture molecules are nucleic acid ligands and the reporter molecules are proteins (page 13, line 24-page 14, line 4).

Regarding Claim 56, Davis et al disclose the method wherein the capture molecule and reporter molecule bind to non-overlapping sites i.e. bind simultaneously to the target (page 13, line 14-page 14, line 13).

Regarding Claim 57, Davis et al disclose the method wherein the reporter molecule binds to a site on the capture molecule:target complex (page 14, lines 7-13).

Regarding Claims 58 and 59, Davis et al disclose the method wherein the substance is a biological fluid e.g. plasma or urine (page 14, lines 20-23).

Regarding Claim 60, Davis et al disclose the method wherein the detection is achieved by flow cytometry (page 13, lines 14-23).

**Additional Comments**

The instant claims are drawn to a method of detecting two or more target compounds. As stated above, because the target coated beads provides a plurality of targets which are then detected, the teachings cited above are encompassed by the instantly claimed two or more targets. The instant claims are not currently limited to two or more different target compounds. However, additional limitations drawn to two or more different targets would not be free of the prior art. Chandler et al (U.S. Patent No. 6,449,562, filed 10 October 1996) teach multiplex ligand detection using flow cytometry (Abstract).

This citation is not considered a rejection because the instant claims are not limited to multiplex detection. This citation is merely provided to facilitate Applicant's understanding of the prior art.

***Double Patenting***

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 29-34, 36-50 and 52-60 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 5,853,984. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method for detecting a target compound comprising the same method steps and differ only in the instant claims are drawn to detecting "two or more target compounds" while the '984claims are drawn to detecting "a target compound". However, the '984 specification exemplifies their method by detecting targets coated onto beads (Column 10, line 64-Column 11, line 4). As such, the patented method detects more than one target i.e. two or more targets as claimed.

**Conclusion**

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this

application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
October 15, 2003